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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,395	09/25/2001	Francis X. Cunningham JR.	P108172-00022	8945

7590 07/09/2003

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1050 CONNECTICUT AVENUE, N.W.
WASHINGTON, DC 20036

EXAMINER
RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application N .	Applicant(s)	
	09/701,395	CUNNINGHAM ET AL.	
	Examin r	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *7 and 8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Application

Claims 1-8 are pending.

Applicant's election with traverse of Group I, claims 1-6 partially drawn to a polynucleotide encoding the polypeptide of SEQ ID NO: 23, vectors and host cells, in Paper No.10, filed on 3/25/2003 is acknowledged.

Applicant's submission of a paper and electronic copy of the sequence listing, and amendments to the specification, in Paper No.12, field on 5/2/2003 is acknowledged.

Applicant's traverse is on the ground(s) that further restriction of the claims based on the claimed nucleotide or amino acid sequences is improper. Applicants submit that according to MPEP § 1850, the Commissioner has waived certain requirements to allow Applicants to claim up to 10 nucleotide sequences that do not have the same or corresponding technical feature. As such, it is Applicant's opinion that the Examiner should have grouped Groups I-III and Groups IV-VI together.

Applicant's arguments have been fully considered but are not deemed persuasive to overcome the restriction requirement. In addition to the arguments presented by the Examiner in Paper No. 9, mailed on 2/25/2003, even if the polynucleotides of Groups I-III or the polypeptides of Groups IV-VI are members of a Markush group, according to PCT Rule 13.2 and to the guidelines in Section (f)(i)(B)(1) of Annex B of the PCT Administrative Instructions, all alternatives of a Markush Group must have a common structure or activity. Although the polynucleotides of Groups I-III encode lycopene ε-cyclases and the polypeptides of Groups IV-VI are lycopene ε-cyclases, neither the polynucleotides of Groups I-III nor the polypeptides of

IV-VI share a common structure. As such, Groups I-VI do not share a special technical feature. In regard to the number of sequences that can be examined in a single application, the guidelines set forth in MPEP §1850 indicate that up to 10 nucleotide sequences that do not have the same or corresponding technical feature can be claimed without the payment of an additional fee. Since there is no provision for examination of additional inventions upon payment of additional fees when the application is the US national stage of a PCT application, the guidelines set forth in MPEP §1850 do not apply. Furthermore, it is noted that MPEP §1850 recites up to 10 and not at least 10 nucleotide sequences will be examined in a single application. In the instant case, since the claims are directed to polynucleotides which encode different proteins, more than 10 polynucleotides are being claimed if one considers that many polynucleotides can encode the same protein in view of the degeneracy of the genetic code.

The requirement is deemed proper and therefore is made FINAL.

Claims 7-8 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

It is noted that the elected claims (1-6) are still partially drawn to non-elected inventions. Examination of such claims will be restricted to the subject matter elected, which in the instant case is a polynucleotide encoding the polypeptide of SEQ ID NO: 23. Applicants are requested to amend the claims accordingly in response to this Office Action.

Specification

1. The specification is objected to because of the following informalities: the address for the American Type Culture Collection (ATCC) listed at page 9, is incorrect and should be replaced with "10801 University Boulevard, Manassas, VA 20110-2209".

2. It is noted that the specification discloses a list of references in pages 24-26. Applicants are advised that if the references cited are to be considered by the Examiner, they have to be submitted in a separate paper, i.e. PTO form 1449. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Priority

3. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 120 or 121 to US application No. 09/088724 filed on 06/02/1998, and 09/088725 filed on 06/02/1998.

4. This application is the national stage of PCT/US99/12121 filed on 06/02/1999

Drawings

5. The drawings have been reviewed and are approved by a draftsperson under 37 CFR 1.84 or 1.152.

Claim Objections

6. Claims 1-6 are objected to because they are drawn in part to a non-elected invention (i.e. polynucleotides encoding the polypeptides of SEQ ID NO: 25 and 26). Claims 1-6 will be interpreted and examined as being directed to the elected invention only, i.e. a polynucleotide encoding the polypeptide of SEQ ID NO: 23, vectors and host cells. Appropriate correction is required.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 1-2 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1-2 are directed to a nucleic acid sequence. As known in the art, a sequence is the graphical representation of the order in which nucleotides or amino acids are arranged in a polynucleotide or a polypeptide. This is analogous to a formula for a chemical compound. It is noted that the instant rejection may be overcome by amending the claims to recite "an isolated ... nucleic acid which...." or similar.

Claim Rejections - 35 USC § 112, Second Paragraph

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claim 1 (claims 2-6 dependent thereon) is indefinite in the recitation of "nucleic acid sequence which encodes for a protein having..." as it is unclear how a sequence encodes a protein. As indicated above, a sequence is a graphical representation. While a nucleic acid sequence can encode an amino acid sequence, a nucleic acid will encode a polypeptide (protein). It is suggested that the term be amended to recite "nucleic acid which encodes for a protein having.." or similar. It is noted that if the suggested language is used, other dependent claims may need to be amended for consistency and proper antecedent basis. See, for example, claims 2 and 3, which recite "nucleic acid sequence of claim 1". For examination purposes, the suggested language will be used in the interpretation of the claims. Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1, 3-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding the polypeptide of SEQ ID NO: 23, does not reasonably provide enablement for a polynucleotide encoding a polypeptide which has at least 85% sequence identity to that of SEQ ID NO: 23. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

Claims 1 and 3 are directed to a polynucleotide which encodes a lycopene ε-cyclase wherein the lycopene ε-cyclase is at least 85% sequence identical to that of SEQ ID NO: 23. Claims 4-6 are drawn to host cells comprising said polynucleotide. While the specification discloses several lycopene ε-cyclases (page 9, line 21, page 10, line17) and discloses which amino acids may be responsible for adding 2 ε rings to form a bicyclic ε-carotene, the specification fails to disclose which are the structural elements which can be substituted, deleted or inserted in a polynucleotide encoding the polypeptide of SEQ ID NO: 23 and obtain an 85% structural homolog which retains lycopene ε-cyclase activity. Moreover, while the specification discloses that conservative substitutions can be made and discloses which regions of the lycopene ε-cyclases may be conserved, there is no disclosure of which are the structural elements in the lycopene ε-cyclase of SEQ ID NO: 23 which can be freely substituted or deleted and still retain activity nor there is disclosure of whether the potential conservative residues correlate with lycopene ε-cyclase function.

While one could argue that the claimed invention is enabled since one can isolate homologs of similar function by structural (i.e. sequence) comparison with the structures

provided by the instant application and/or the prior art, the state of the art teaches how small structural changes can result in major changes in function. Witkowski et al. (Biochemistry 38:11643-11650, 1999) teaches that one amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* where found to be hydroxylases once tested for activity. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Broun et al. (Science 282:1315-1317, 1998) teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase. Even the specification teaches that substituting 5 amino acids can change the product specificity of a lycopene ε-cyclase from ε,ψ-carotene to bicyclic ε-carotene (page 9, lines 30-32). Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the structural elements required to maintain the desired function, and the unpredictability of the prior art in regard to structural changes and their effect on function, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to screen and isolate those polynucleotides, as encompassed by the claim, with the desired function. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Allowable Subject Matter

14. A polynucleotide encoding the polypeptide of SEQ ID NO: 23, vectors and host cells comprising said polynucleotide, appear to be free from the prior art.

Conclusion

15. No claim is in condition for allowance.

16. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

17. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
June 12, 2003

REBECCA E. PRUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600